MEDICAL PROCEEDINGS

MEDIESE BYDRAES

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EDITORIAL · REDAKSIONEEL

ALLEGATIONS OF MEDICAL NEGLIGENCE

AN ORANGE FREE STATE CIVIL ACTION

Towards the end of last year an interesting action* was heard in the Orange Free State Provincial Division of the Supreme Court of South Africa. The plaintiff sued a pharmacy and a medical practitioner for £20,000 damages, alleged to have followed the use of Cafergot pills† for the treatment of migraine.

The plaintiff's case rested on the following allegations:

(*a*) Cafergot pills can only be used with safety if not more than 6 pills are taken in 2 hours on any one day with a maximum of 10 per week.

(*b*) The use of more pills has a seriously prejudicial effect on the human system.

(*c*) Both defendants should have known this by reason of their respective professions.

(*d*) The plaintiff herself did not know this.

(*e*) The first defendant was negligent in

i. Neglecting to indicate on the instructions that not more than 10 pills per week should be taken by the plaintiff;

ii. Indicating on the instructions that the plaintiff take 2 pills at once and then one every half hour for 6 hours.

(*f*) The second defendant was negligent in

* Pienaar *vs* Voortrekker-apteek and Dr. M. J. Goddefroy, November 1956.

† Cafergot tablets contain 100 mg. caffeine and 1 mg. ergotamine tartrate.

BEWERINGS IN VERBAND MET MEDIESE NALATIGHEID

'N SIVIELE AKSIE IN DIE ORANJE VRYSTAAT

Teen die einde van verlede jaar het 'n interessante saak* in die Vrystaatse Provinsiale Afdeling van die Hooggeregshof van Suid-Afrika gedien. Die eiseres het 'n apteek en 'n mediese praktisyn gedagvaar vir £20,000 skade wat, na beweer is, gevolg het op die gebruik van Cafergot-pille† vir die behandeling van migraine.

Die eiseres se saak het op die volgende bewerings berus:

(*a*) Cafergot-pille kan slegs met veiligheid gebruik word as nie meer as 6 pille binne 2 uur op enige een dag geneem word nie, met 'n maksimum van 10 per week.

(*b*) Die gebruik van meer pille het 'n ernstig skadelike effek op die menslike gestel.

(*c*) Albei verweerders behoort hiervan bewus te gewees het uit hoofde van hul onderskeie beroepe.

(*d*) Die eiseres self was nie hiervan bewus nie.

(*e*) Die eerste verweerder was nalatig toe hy

i. Versuim het om op die instruksies aan te dui dat die eiseres nie meer as 10 pille per week behoort te neem nie;

* Pienaar *teen* Voortrekker-apteek en dr. M. J. Goddefroy, November 1956.

† Cafergot-tablette bevat 100 mg. kaffeïen en 1 mg. ergotamien-tartraat.

i. Neglecting to indicate in the prescription that the plaintiff should not take more than 10 pills in one week;

ii. Instructing the plaintiff that she could take 2 at once and then 1 each half hour for a total of 6; and

iii. Instructing that she could repeat the prescription 20 times without any limitations as to time.

(*g*) In consequence of such negligence on the part of both defendants or alternatively on the part of either of them, the plaintiff took

5 pills on 5 September 1954;
4 pills on 22 September 1954;
4 pills on 30 September 1954, 2 at 2 p.m., one at 2.30 and one at 3 p.m.;
2 pills on 1 October 1954 (2 in the evening);
2 pills on 2 October 1954 (2 in the evening);
6 pills on 3 October 1954 (2 at 2 p.m., one at 2.30, one at 3, one at 3.30 and one at 4 p.m.).

(*h*) In consequence of having taken more than 10 in a week, her body was severely injured, and she suffered acute *ergot* poisoning.

The bodily injury and poisoning were alleged to have caused permanent injury to her eyes *and* sight and to her general health, more particularly in that:

i. Her general health was greatly weakened;

ii. Her sight was damaged and both eyes injured to such an extent that vision in both eyes was seriously impaired;

iii. She still suffered pain in both eyes (on 29 September 1955);

iv. Her digestive organs were affected by the poisoning, and she still suffered pain in this connexion (on 29 September 1955);

v. Her nervous system was affected.

(i) The plaintiff discovered the poisoning shortly after 4 p.m. on 3 October 1954.

It was not suggested by the plaintiff at any stage that the amount of caffeine taken by her had led to any ill effects. Her claim rested on the fact that the pills contained ergotamine tartrate which led her to suffer from acute *ergot* poisoning, the main result of which was the production of cataracts in both eyes.

There was some difference in phraseology between the instructions on the label and those written by the doctor on the prescription,* but it was conceded by an expert witness called by the plaintiff that it would not have been unreasonable in the circumstances for the dispenser to have written the instructions that he did. It was also conceded by the plaintiff's expert witnesses in cross-examination that it was not reasonable to expect a pharmacist to be acquainted with such a fact (if it was a fact), that not more than 10 Cafergot pills should have been taken in any one week. The allegations of negligence against the pharma-

* The medical practitioner had prescribed '2 at once and then one each half hour for a total of 6'. This was dispensed as '2 at once and then one every half hour for a total of 6 hours'.

ii. Op die instruksies aangedui het dat die eiseres dadelik 2 pille moet neem, en daarna een elke halfuur in 'n tydperk van 6 uur.

(*f*) Die tweede verweerder was nalatig toe hy

i. Versuim het om in die preskripsie aan te dui dat die eiseres nie meer as 10 pille in een week behoort te neem nie;

ii. Opdrag aan die eiseres gegee het dat sy dadelik 2 tablette moet neem, en dan 1 elke halfuur totdat altesaam 6 geneem is; en

iii. Die eiseres meegedeel het dat sy die preskripsie 20 keer kon herhaal sonder enige beperkings wat tyd betref.

(*g*) Ten gevolge van sodanige nalatigheid aan die kant van albei verweerders, of, as alternatief, aan die kant van een van beide, het die eiseres die volgende geneem:

5 pille op 5 September 1954;
4 pille op 22 September 1954;
4 pille op 30 September 1954, 2 om 2 nm., een om 2.30 en een om 3 nm.;
2 pille op 1 Oktober 1954 (2 in die aand);
2 pille op 2 Oktober 1954 (2 in die aand);
6 pille op 3 Oktober 1954 (2 om 2 nm., een om 2.30, een om 3, een om 3.30 en een om 4 nm.).

(*h*) Ten gevolge van die feit dat sy meer as 10 binne 'n week geneem het, is haar liggaam ernstig benadeel en het sy aan akute *ergot*-vergiftiging gely.

Die liggaamlike benadeling en vergiftiging het, na beweer is, permanente beskadiging van haar oë en gesigsvermoë sowel as van haar algemene gesondheid tot gevolg gehad, in besonder deurdat:

i. Haar algemene gesondheid aansienlik verswak is;

ii. Haar gesigsvermoë beskadig en albei oë in so 'n mate beseer is dat die gesig van albei oë ernstig belemmer is;

iii. Sy nog steeds aan pyn in albei oë ly (op 29 September 1955);

iv. Haar spysverteringsorgane deur die vergiftiging geaffekteer is en sy in hierdie verband nog steeds aan pyn gely het (op 29 September 1955);

v. Haar senuweestelsel aangetas is.

(i) Die eiseres het die vergiftiging kort na 4 nm. op 3 Oktober 1954 ontdek.

Op geen stadium is daar deur die eiseres beweer dat die hoeveelheid kaffeïen wat sy geneem het, enige nadelige effek gehad het nie. Haar eis het berus op die feit dat die pille ergotamien-tartraat bevat het, en dat dit die rede was waarom sy aan akute *ergot*-vergiftiging gely het. Die vernaamste gevolg hiervan was die ontwikkeling van pêrels op albei oë.

Daar was 'n verskil in bewoording tussen die instruksies op die etiket en dié wat deur die dokter in die preskripsie neergeskryf is,*

* Die mediese praktisyn het ‚2 dadelik en dan een elke halfuur vir 'n totaal van 6' voorgeskryf. Dit is toeberei as ‚2 dadelik en dan een elke halfuur vir 'n totaal van 6 uur'.

cist were accordingly refuted.

The medical side of the plaintiff's case rested mainly on the alleged production of bilateral cataracts claimed to have been a result of acute *ergot* poisoning following the ingestion of Cafergot. Since Cafergot contains not ergot but ergotamine, there was here clearly a serious confusion between *acute ergot poisoning* and *acute ergotaminism*. This distinction is not academic because the crystalline alkaloid ergotamine has not got all the pharmacological actions of crude ergot, which is a mixture of many alkaloids and other substances besides ergotamine.

The plaintiff's experts were challenged to produce a single case of cataract following the use of either ergotamine or Cafergot. They were unable to mention any such cataractous complication. Indeed, the cross-examination made it clear that the defendants' experts were prepared to testify that there was no such recorded case and that it was not a complication which ergotamine or Cafergot could produce.

The plaintiff's experts based their opinions about the possible production of cataract by ergotamine on the records of cataract which had occurred during epidemics of acute ergot poisoning in Central and Eastern Europe during the 19th century. It was established in cross-examination that such cataracts had not been described in epidemics in Western Europe and that the views of the plaintiff's experts depended upon an alleged association between ergot and cataracts confined to the 19th century. It was pointed out to the plaintiff's witnesses that even if there were such an association, it raised a presumption that the toxic agent producing cataracts in epidemics of acute ergot poisoning was unlikely to have been ergotamine, because although ergot grown in Western Europe (where cataract had not been described) contained very large amounts of ergotamine, the ergot in Central and Eastern Europe (where cataract had been described in ergot epidemics) contained no ergotamine.

The plaintiff's experts offered an explanation of how ergotamine could produce a cataract. They averred that ergot and ergotamine, by constricting the blood vessels of the eye, could interfere with the composition of the aqueous and so affect the nutrition of the lens with the production of a cataract. This hypothesis did not fare too well under cross-examination, during which it was indicated to the Court that the theory was wholly untenable in the

maar 'n deskundige getuie wat deur die eiseres opgeroep is, het toegegee dat dit in die omstandighede nie onredelik vir die apteker sou gewees het om die instruksies neer te skryf wat hy in werklikheid neergeskryf het nie. Tydens kruisverhoor is daar ook deur die eiseres se deskundige getuies toegegee dat dit nie redelik is om te verwag dat 'n apteker kennis moet dra van die feit (as dit 'n feit was) dat nie meer as 10 Cafergot-pille binne 'n enkele week geneem moet word nie. Die bewerings van nalatigheid teen die apteker is derhalwe weerlê.

Die mediese sy van die eiseres se saak het hoofsaaklik berus op die beweerde ontwikkeling van pêrels op albei oë ten gevolge van akute *ergot*-vergiftiging volgende op die inneming van Cafergot. Aangesien Cafergot nie ergot nie maar wel ergotamien bevat, was hier duidelik 'n ernstige verwarring tussen *akute ergot-vergiftiging* en *akute ergotaminisme*. Dit is nie 'n bloot akademiese verskil nie, want die kristalagtige alkaloïed ergotamien het nie al die farmakologiese effekte van ruwe ergot nie. Ruwe ergot is 'n mengsel van talle alkaloïede en ander stowwe, behalwe ergotamien.

Die eiseres se deskundiges is uitgedaag om 'n enkele geval op te noem waar 'n pêrel op die oog op die gebruik òf van ergotamien òf van Cafergot gevolg het. Hulle was nie in staat om so 'n katarak-ontwikkeling aan te dui nie. Trouens, tydens die kruisverhoor het dit duidelik geword dat die verweerder se deskundiges bereid was om te getuig dat daar geen sodanige aangetekende geval was nie, en dat dit nie 'n verwikkeling is wat deur ergotamien of Cafergot geproduseer kan word nie.

Die eiseres se deskundiges het hul menings oor die moontlike produksie van 'n oogpêrel deur ergotamien gebaseer op die aantekenings i.v.m. oogpêrels wat voorgekom het tydens epidemieë van akute ergotvergiftiging in Sentraal- en Oos-Europa tydens die 19de eeu. Tydens kruisverhoor is daar vasgestel dat sodanige oogpêrels nie beskryf is in epidemieë in Wes-Europa nie, en dat die sienswyses van die eiseres se deskundiges afgehang het van 'n beweerde verband tussen ergot en oogpêrels wat tot die 19de eeu beperk was. Die eiseres se getuies is toe daarop gewys dat selfs indien daar so 'n verband bestaan, dit aanleiding gee tot die veronderstelling dat die giftige stof wat oogpêrels tot gevolg gehad het tydens epidemieë van akute ergotvergiftiging waarskynlik nie ergotamien was nie, want hoewel die ergot wat in Wes-Europa gekweek word (waar oogpêrels nie beskryf is nie) besonder groot

view of the defendant's experts who would testify that the action of ergot on the blood vessels of the eye was not the same as the action of ergotamine. The plaintiff's experts were unable to deny this or to deny that ergotamine had a totally different action on the branches of the *internal* carotid artery from what it had on the branches of the *external* carotid artery. Egotamine is effective in the treatment of true migraine because, by constricting the branches of the *external* carotid, it diminishes the pulsations in those arteries and so relieves the migrainous headache. Evidence available indicates that ergotamine does not constrict the branches of the *internal* carotid artery or the retinal arterial supply and may, in fact, even dilate these vessels and improve the blood supply to the brain. In the light of these considerations it is difficult to appreciate the pharmacological or other scientific foundation for a hypothesis that ergotamine could produce cataracts.

It was also pointed out that following the ingestion of ergotamine, this substance normally appeared in the aqueous surrounding the lens. Despite this, no case of cataractous damage to the human lens has yet been described, although millions of tablets containing ergotamine have been consumed in the last 35 years.

Cross-examination of the plaintiff's experts (who included only one medical practitioner —an ophthalmologist), made it clear that the literature abounded with numerous references establishing beyond any doubt that many more tablets than 10 per week could be taken for much longer periods than one week without any deleterious effects. Reports, for example, were quoted in which 1 mg. of ergotamine had been used 3 times a day (i.e. 21 tablets per week) for as long as 6 months without any harm to the patient.

The additional interesting observation was also brought to light that the plaintiff had in fact suffered from cataracts in both eyes in 1950, i.e. 4 years before she took the first Cafergot tablet.

The net effect of the very severe cross-examination to which the plaintiff's experts were subjected, was to destroy completely any medical basis for the plaintiff's allegations.

Towards the end of the second week of the trial she withdrew her action against both defendants and also agreed unconditionally to withdraw all allegations of negligence against them. On her behalf her counsel stated that

hoeveelhede ergotamien bevat, bevat die ergot van Sentraal- en Oos-Europa (waar oogpêrels wel tydens ergot-epidemieë beskryf is) geen ergotamien nie.

Die eiseres se deskundiges het geprobeer om te verduidelik hoe ergotamien 'n oogpêrel kan produseer. Hulle het beweer dat ergot en ergotamien die bloedvate van die oog saamtrek en derhalwe 'n belemmerende effek op die samestelling van die wateragtige vog het, ten gevolge waarvan die voeding van die lens geaffekteer en 'n oogpêrel geproduseer word. Hierdie veronderstelling het nie te goed gevaar tydens kruisverhoor nie, in die loop waarvan daar aan die Hof verduidelik is dat hierdie teorie heeltemal onhoudbaar is volgens die mening van die verweerder se deskundiges wat bereid was om te getuig dat die effek van ergot op die bloedvate van die oog nie dieselfde as die effek van ergotamien was nie. Die eiseres se deskundiges kon dit nie ontken nie. Ook kon hulle nie ontken nie dat die effek van ergotamien op die takke van die *binne*kopslagaar heeltemal anders is as die effek daarvan op die takke van die *buite*kopslagaar. Ergotamien is doeltreffend vir die behandeling van suiwer migraine omdat dit die takke van die *buite*kopslagaar vernou en daardeur die klopping in daardie slagare verminder en gevolglik die migraine-hoofpyn verlig. Die beskikbare getuienis dui daarop dat ergotamien nie die takke van die *binne*kopslagaar vernou of die lewering van slagaarbloed aan die oognetvlies verminder nie. Trouens, dit kan hierdie bloedvate laat uitsit en gevolglik die lewering van bloed aan die brein verbeter. Met die oog op hierdie oorweging is dit moeilik om die farmakologiese of ander wetenskaplike gronde vir die veronderstelling dat ergotamien oogpêrels kan produseer, te begryp.

Daar is ook gewys op die volgende: Na die inneming van ergotamien verskyn hierdie stof normaalweg in die wateragtige vog waarvan die lens omring is. Desondanks is geen geval van katarak-beskadiging van die menslike lens tot dusver beskryf nie, hoewel miljoene ergotamientablette gedurende die afgelope 35 jaar geneem is.

Die kruisverhoor van die eiseres se deskundiges (onder wie daar slegs een mediese praktisyn—'n oftalmoloog—was) het aan die lig gebring dat daar in mediese publikasies talle verwysings is wat bo alle twyfel bewys dat veel meer as 10 tablette vir veel langer tydperke as 'n week geneem kan word sonder dat dit enige nadelige effek het. Daar is bv. verslae oor gevalle waar 1 mg. ergotamien 3 maal per dag gebruik is (d.w.s. 21 tablette per week) vir 'n tydperk van soveel soos 6 maande sonder dat dit enige nadelige effek op die pasiënt gehad het.

'n Addisionele interessante waarneming het ook

she was satisfied that there had been no negligence or breach of professional or other duties on the part of either the pharmacist or the doctor. Indeed, she apologized for any inconvenience the allegations might have caused to either of the defendants.

She also accepted the opinion of the defendants' experts that the use of Cafergot tablets had not affected her and admitted that she had in fact suffered from cataract in 1950 before she had ever used Cafergot pills.

It is our view that this was a very proper conclusion to the trial. No doubt the plaintiff instituted her action in good faith, but it is important to recognize that both defendants were completely vindicated in their decision to defend the claim against them as a matter of principle. Their public spirited action has done much to prevent professional men from finding themselves in such predicaments in the future. Moreover, in view of the established value of Cafergot or ergotamine in the management of an incapacitating condition such as migraine, the defendants have added to their public services by vindicating also the safety of this drug for the conditions in which it is indicated. It would have been disastrous if those many hundreds of thousands of patients suffering from migraine or any other form of vascular headache should have been allowed to develop an entirely falsely grounded fear about the use of this valuable and effective remedy.

aan die lig gekom, nl. dat die eiseres in werklikheid in 1950 aan pêrels op albei oë gely het, d.w.s. 4 jaar voordat sy die eerste Cafergot-tablet geneem het.

Die netto-effek van die besonder deurtastende kruisverhoor waaraan die eiseres se deskundiges onderwerp was, was die algehele vernietiging van enige mediese basis vir die eiseres se bewerings.

Teen die einde van die tweede week van die verhoor het sy haar aksie teen albei verweerders teruggetrek en onvoorwaardelik ingestem om ook alle bewerings van nalatigheid teen hulle terug te trek. Haar advokaat het namens haar aangekondig dat sy tevrede is dat daar geen nalatigheid of oortreding van professionele of ander pligte aan die kant van die apteker of die dokter was nie. Trouens, sy het verskoning gevra vir die ongerief wat die bewerings bes moontlik vir een of albei verweerders meegebring het.

Sy het ook die mening van die verweerders se deskundiges aanvaar, nl. dat die gebruik van Cafergot-tablette haar nie geaffekteer het nie, en sy het erken dat sy inderdaad aan pêrels op die oë gely het in 1950 voordat sy ooit Cafergot-pille gebruik het.

Volgens ons mening was dit 'n baie behoorlike manier vir die saak om te eindig. Die eiseres het haar aksie sonder twyfel te goeder trou ingestel, maar dit is van belang om daarop te let dat albei verweerders volkome geregverdig was om haar eis as 'n beginselsaak te bestry. Hul optrede getuig van burgersin, en het veel gedoen om te voorkom dat professionele manne hulle in die toekoms in 'n dergelike moeilike posisie bevind. Temeer, met die oog op die erkende waarde van Cafergot of ergotamien by die behandeling van 'n onbekwaammakende toestand soos migraine, het die verweerders die diens wat hulle aan die publiek bewys het, nog verder vergroot deur aan te toon dat hierdie middel veilig is vir die toestande waarvoor die aangedui word. Dit sou rampspoedig gewees het as daar by die honderdduisende pasiënte wat aan migraine of enige ander vorm van bloedvaat-hoofpyn ly, 'n heeltemal ongegronde vrees oor die gebruik van hierdie waardevolle en doeltreffende middel ontstaan het.

STANDARDIZED OPERATIONS

GASTRECTOMY

A. LEE MCGREGOR, F.R.C.S. (ENG.), M.CH. (EDIN.)
Johannesburg

(*Continued from p.* 98)

The Drainage Jejunostomy. The Allen (1944) procedure[2] of draining the stomach stump by a catheter has decided advantages:

(1) Gravity drainage gives complete assurance that pressure is not building up in stomach and duodenum with the attendant risks of putting tension on the anastomosis and the closed duodenal end.

(2) The patient is saved the considerable discomfort and occasional risks of a tube into the stomach via the nose.

(3) The tube is a valuable ally in the rare case when the gastro-jejunal stoma becomes blocked by oedema about the 8th to the 12th day.

(4) There is little risk attached to the use of the procedure. When the author first used the method, 2 cases of intestinal obstruction

developed, due to small gut passing between the anterior abdominal wall and the anchored jejunal loop.

The matter was discussed with Dr. Arthur Allen, of Boston, who stated that in 1,000 gastrectomies using the jejunostomy there had been no complication. The author feels that the obstructions which occurred in his practice were due to errors in technique and there has been no further difficulty since these have been corrected.

Steps in the Procedure.

(*a*) The jejunum is picked up about 8″ from the duodeno-jejunal flexure. The assistant holds it in 2 hands; a purse string atraumatic suture chromic 000 catgut on a straight needle is inserted. The assistant holds this suture, the 2 ends in one hand and the distal loop in the other; a puncture is made with a tenotomy knife in the centre of the gut, which is encircled by the suture. A No. 16 Wishart catheter on a straight, lubricated introducer is passed through the puncture and guided through the anastomosis well up into the stomach stump. Patience is required in this procedure as the tip of the catheter may be caught in a jejunal fold or the anastomosis suture line. The purse string is then tightened and tied, and the catheter is transfixed by the needle and fixed in place. A second purse string using plain catgut is inserted (Fig. 24).

(*b*) The catheter is passed through the greater omentum. A stab wound is made through the abdominal wall at the outer border of the left rectus at the umbilical level. A pair of Spencer Wells' forceps is pushed through the abdominal wall and grips the end of the catheter, which is pulled through the abdominal wall until the bowel lies in contact with the peritoneum. The catheter is fixed with a skin stitch, the ends of which are twisted round the catheter and tied (Fig. 25). The surgeon then passes his hand to the stomach and checks that the catheter is in this organ. If it has slipped out, the skin stitch is cut, the catheter withdrawn and the procedure repeated.

(*c*) In all cases where gastrectomy has been done for cancer and in patients with poor veins a second jejunostomy is carried out in the same way, about 2″ distal to the first. This is for feeding purposes.

If it is preferred, the jejuno-gastrostomy tube is dispensed with and suction applied to a thin tube passed into the stomach through the nose.

The author feels that there is never the same security attendant on this alternative procedure. In fact, a false sense of security is engendered. The tube occasionally is not in the stomach, and the ordinary bottle type of suction is associated with a definite mortality.

Closure of the Abdomen. The peritoneum is closed with 0 plain catgut on an atraumatic needle; at every inch of the suture line a re-inforcing suture of similar material is inserted and tied (Fig. 26).

The closure of fascia is dependent on the disease and the exposure. In carcinoma the closure is with continuous stainless wire, gauge 32, and the same technique is used for midline incisions, the linea alba being approximated by near-far, far-near continuous sutures (Fig. 27).

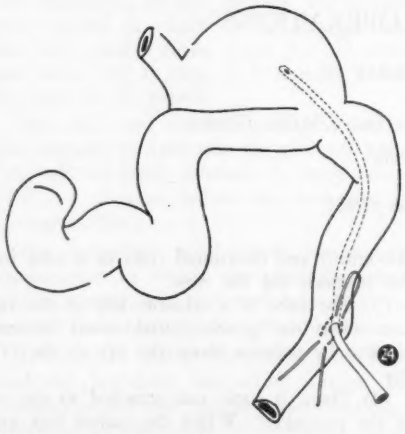

Fig. 24. Detail of the jejunostomy.

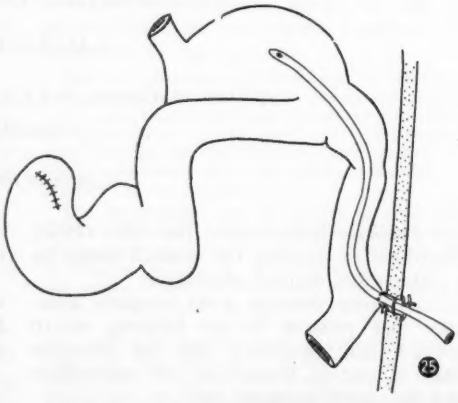

Fig. 25. Completion of the drainage jejunostomy.

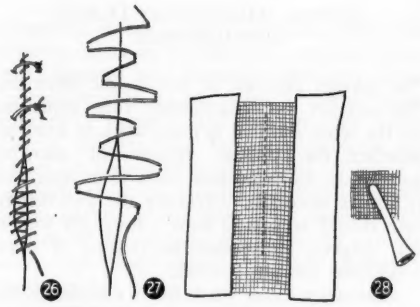

Fig. 26. Closure of the peritoneum.
Fig. 27. Fascial closure with far near, near far steel wire.
Fig. 28. Operation completed.

When a rectus-displacing exposure has been used, the anterior sheath may be closed with wire, or with cotton or linen No. 60 using interrupted sutures spaced ¼″ apart, the knots being tied *within* the fascia.

The use of stainless steel wire is an advance. It is strong and quite non-irritating. It has been used in recent years both in hospital and in private practice by the writer and his assistants for both herniae and abdominal closure. Thus far there has been no complication. The principles in its application are:

(*a*) Avoidance of kinking.
(*b*) A bloodless field.
(*c*) No tension.

The skin is sutured with cotton or linen thread No. 60 spaced ½″ apart. Endeavour is made to tie so that there is a 1 mm. gap between the co-apted edges. Two or three of the sutures pick up the underlying sheath, and are intended to obliterate the potential 'dead space' between sheath and fat, thus obviating the formation of collections of blood and serum. These deep stitches are tied while the assistant has a finger in the bight of the suture. No stitches are tightly tied.

The Dressing. No antiseptic is applied. Mastisol is painted round the wound and a roll of gauze dressing 12 layers thick is put on the wound, and fixed with adhesive strapping—leaving a strip of gauze exposed for evaporation. If this is not done the wound becomes sodden (Fig. 28).

After-Treatment. The patient is given Omnopon gr. ⅓ as required. His position is changed 4-hourly. The foot of the bed is raised on 6″ blocks. He is encouraged to breathe deeply and to move his limbs around freely. A monkey chain is attached to the bed and he uses his arms to raise himself, thus avoiding strain on the abdominal muscles.

Alimentation. A blood transfusion is given as a routine on the table. It is strongly felt that the blood picture should be normal before operation. The practice of operating on anaemic patients with the intention of correcting the deficiency during operation is unsound; 500 c.c. of blood may be adequate, but more is given if required. 5% dextrose in water is given by drip at the rate of 30 drops per minute. To each 1,000 c.c. Vacoliter are added 60 c.c. of absolute alcohol. This has a sedative effect and, together with glucose, the daily calorie requirements are supplied, thus reducing protein breakdown to a minimum. It is not usually necessary to supply amino acids, but in exceptional cases they may be given and can be used by the body as proteins, provided the calorie requirements have been adequately supplied by glucose and alcohol, as outlined above.

Fluids: *Intravenous.* A careful intake and output chart is kept. On the operation day 2,000 c.c. of fluid are usually sufficient. Thereafter it is a matter of calculation. The required intake is assessed thus—losses by vomiting, by jejunostomy tube, by urine and by insensible loss for the previous 24 hours represent the needs for the ensuing day. This need is supplied by 5% dextrose in water + alcohol + vitamins A, B and C. Care is taken to see that 1,400 calories are administered.

Electrolytes: The kidneys retain sodium but not potassium. Sodium loss does not begin for about a week, whereas potassium chloride loss begins at once; 4 g. of potassium chloride are therefore given daily by Vacoliter. Salt (sodium chloride) is given according to the loss by vomiting or jejunostomy tube; vomiting does not occur. If 500 c.c. are lost by tube, it is considered to be half isotonic and the same is true of insensible loss. Thus half as much isotonic salt solution is given as is lost by the total of the tube drainage and the insensible loss. Any balance either way is added to or subtracted from the requirements for the ensuing day.

Fluids: *Oral.* On the day following operation the patient is allowed a 2-oz. medicine glass of fluid by mouth per hour; after that there is no restriction on the fluid intake. From the fourth day milk and other light foods are taken. A week after the operation the patient may be allowed a grill and thereafter the diet is liberal.

Management of the Jejunostomy Tube. The

jejunostomy catheter is attached to a Gomco electric suction pump which leads into a Winchester bottle on the floor. The drainage is blood-stained for 24 hours. The catheter is detached from the suction apparatus 4-hourly and irrigated with a few c.c. of sterile saline to dislodge blood clot or tenacious mucus. When the fluid sucked from stomach is less than that taken by mouth—usually after 3 or 4 days—the electrical suction is discontinued and the gravity suction broken by inserting a Y-glass piece on the tube leading from catheter to the Winchester. One limb of the glass tube goes to the jejunostomy catheter, one goes to the Winchester and the third is open to air. The Y-connexion is fixed to the head of the bed at the level of the patient's stomach (Fig. 29).

Intra-gastric pressure is thus prevented from reaching a level which is uncomfortable to the patient or dangerous to the suture lines. Should the patient complain of gastric fulness, the level of the Y-piece with attached tubes is lowered. About the 7th or 8th post-operative day the jejunostomy catheter is closed with a spigot, which is removed if gastric fulness is complained of. The catheter is removed when the stitches come out on the 10th day. There is trifling oozing from the puncture wound for a day or so.

The writer has seen 2 cases in his Hospital Unit where gastric discomfort has persisted up to the time of suture removal. This is due to oedema of the gastro-jejunostomy stoma, which is maximal at the 10th day. In such circumstances the jejunostomy catheter is a valuable ally as a decompression mechanism. The catheter is left in place till the oedema subsides.

GENERAL MANAGEMENT DURING CONVALESCENCE

The patient gets out of bed on the third day. The stitches and gastrostomy tube come out on the tenth day. It is quite open to question whether the present fashion of allowing patients to leave hospital soon after operation is always advisable. Certainly the gastrectomy case should remain at least a fortnight following surgery, and sometimes longer if home conditions are not suitable.

Abstention from work for 3 months should be insisted on. The patient takes 6 meals a day, as he feels bloated on taking a relatively small meal. There are few restrictions on diet. Condiments and highly spiced dishes are avoided. He should not drink with meals. This regime continues for 3 months.

Eighty per cent and more of adequately performed gastrectomies have achlorhydria after operation. Furthermore, the mechanics of digestion are radically altered, food being directed straight into jejunum by the gastric remnant which acts as a funnel (Fig. 30).

As a result of these factors intestinal organisms find their way into and flourish in the stomach. This further upsets the digestive processes. One effect of the achlorhydria and foreign flora in the stomach is that vitamins —especially the B group—are utilized by the

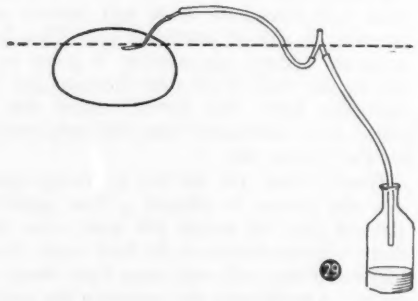

Fig. 29. This figure is meant to show on the reader's left the level of the jejunostomy catheter in the patient's stomach and on the right is the Y connexion breaking the suction and elevated to stomach level.
Fig. 30. The funnel.

organisms in the stomach and the patient may develop signs of avitaminosis, angular stomatitis, glossitis, etc. Aneurine deficiency results in considerable muscle pain. It should therefore be a routitne that patients take hydrochloric acid in the form of Aklorep—one tablet on sitting down to a meal. Vitamin B is taken after the meal. This regime should be continued indefinitely. Six months after operation the patient may take an ordinary diet. He may smoke and use alcohol in moderation.

Gastrectomy is a serious procedure. If it is done in properly selected cases, the patient has the right to expect to live a normal life following surgery.

PREPYLORIC SECTION: THE BANCROFT PROCEDURE

When the abdomen is opened the duodenal area is inspected. If conditions are such that division of the duodenum would be hazardous or its closure uncertain, the section should be proximal to the pylorus. The steps of the procedure are:

1. The curvatures of the stomach are mobilized as usual by securing and dividing vessels.
2. The stomach is divided proximally.
3. The site of distal division of the stomach is 4 finger breadths proximal to the pyloric veins (veins of Mayo). Care is necessary here that enough of the pyloric antrum is left for satisfactory inversion and closure. The beginner is apt to cut away too much stomach.
4. The open end of the pyloric antrum is grasped by 4 pairs of Allis forceps placed at the cardinal points of the compass.
5. The mucosa is grasped with mosquito forceps and dissected from the muscularis, all vessels being secured and tied with 3-0 plain catgut. The process is tedious and much care is necessary not to tear or puncture the muscle. The dissection is continued to the pyloric sphincter. The cuff of mucosa is cut away. It is *not* tied across, as this would lead to retension of blood in a closed space, which would endanger the suture line.
6. The open end of the pyloric antrum is now closed by 2 layers of catgut which produce inversion so that serosa is applied to serosa. This is supplemented by a layer of interrupted linen (No. 60) mattress sutures.
7. The further steps of the operation are as described.

In the experience of the writer this operation is entirely satisfactory.

REPORT ON A SERIES OF CASES OPERATED ON FOR PEPTIC ULCER

Seventy-six private cases underwent gastrectomy from September 1938 to October 1951. Until quite recently gastro-enterostomy was the treatment of choice for peptic ulcer. Thus of the cases mentioned the vast majority have been done between 1948 and 1951.

A questionnaire was sent to these cases—48 replied. Many of the others are known to be well, but they are not included as the data are incomplete.

Sex Incidence: Males 38; Females 10.

Age Incidence: Oldest 72; Youngest 20; Average 49.7.

Pathology Found at Operation:

Gastric ulcer	7 cases.
Stomal ulcer	2 cases.
Gastro-jejuno-colic fistula ...	1 case.
Hypertrophic gastritis	1 case.
Duodenal ulcer	37 cases.

One case of duodenal ulcer in a man of 20 years was a 'middle of the night' emergency in which partial gastrectomy was undertaken for uncontrollable bleeding from a chronic ulcer.

Type of Operation Carried Out: The ¾-gastrectomy described above was carried out with the following departures from the routine procedure.

(*a*) Prepyloric section with the removal of mucous membrane of the antral stump was done in 7 cases, because conditions at the duodenum would have made its closure hazardous.

(*b*) The gastro-jejunal anastomosis was of the posterior no-loop type in 46 cases. It was made with a short anterior loop in 2 cases because of shortness or scarring of the mesocolon.

(*c*) Cholecystectomy for chronic cholecystitis and cholelithiasis was combined with gastrectomy in 2 cases.

(*d*) Pyloric obstruction of severe degree was present in 3 cases.

Complications: There were no chest complications, neither did thrombophlebitis occur. There was no sepsis of any kind and wounds healed by first intention. The abdomen had to be re-opened in 3 cases.

Case 1. The gastrectomy had to be revised on the evening of the day of operation for exsanguinating haemorrhage. This was due to inadequate suturing.

Case 2. In one case the patient developed severe shock 4 days after gastrectomy. Exploration disclosed a closed loop obstruction involving several feet of small bowel which necessitated resection. It was due to a congenital band.

Case 3. The remaining case was one of obstruction of the afferent loop. Exploration was carried out and the gastrectomy revised.

These 3 cases made good recovery and have remained well.

Operative Mortality: There was one death in this series of 76 cases, an operative mortality of 1.3%.

The single death concerns an elderly male aged 67, with 20 years' dyspeptic history. He was generally a poor risk with defective kidney function and marked calcification of the great vessels. Operation was difficult, but not unusually so. The writer left for overseas soon after the operation. Apparently the patient went downhill rapidly and died of exhaustion and inanition.

From the end of 1951 until the end of June 1956 an additional 78 gastrectomies have been done for ulcer. Three of these were for exsanguinating haemorrhage. The single death occurred in a man 52 years old who had had the Smithwick operations for hypertension carried out one year before. He was bled out when seen and despite restorative measures he died soon after operation. In the total series of 154 gastrectomies for gastric or duodenal ulcer there have been 2 deaths—a mortality of 1.3%.

FOLLOW UP OF CASES WHO REPLIED TO THE QUESTIONNAIRE

(NUMBER OF CASES 48)

Question 1. Has your operation been very suecessful, successful or unsuccessful?

Very successful: 41; Successful, 7; Unsuccessful: 0.

Question 2. Are you on a normal or a restricted diet?

Normal diet: 48; Restricted diet: 0.

Question 3. Are you smoking?

Smokers: 33; Non-smokers: 15.

Question 4. Do you take alcohol?

Taking alcohol: 34; Not taking alcohol: 14.

Question 5. How has your weight behaved?

Gained weight: 23; Stationary: 14; Lost weight: 11.

Question 6. Have you any complaints relative to your operation?

No complaint: 38; Complaint: 10.

ANALYSIS OF COMPLAINTS

Case No.

9. Sometimes troubled with belching and indigestion.
17. Sometimes troubled with epigastric discomfort, nausea and loose bowels.
19. Occasionally has ' acid '.
25. Sometimes has mild indigestion.
26. Occasional abdominal pain.
40. Occasional discomfort after a large meal. This is getting better.
42. Cannot take a big meal.
43. Mild discomfort after breakfast; with a small breakfast there is no discomfort.
46. Tired after meals.
47. Occasional nausea.

There has been no case of dumping syndrome in the popularly accepted significance of the term. All patients considered that surgery had been worthwhile.

CONCLUSIONS

1. In properly selected cases gastrectomy gives gratifying results.
2. The routine procedure was a retrocolic no-loop anastomosis.
3. Drainage of the stomach stump by routine jejunostomy enhances the post-operative comfort of the patient and adds to the safety of the operation.
4. The operation has a low mortality—1.3% in 154 cases, which included emergency gastrectomy for uncontrollable bleeding.

OPSOMMING

1. In behoorlik uitgesoekte gevalle kan gastrektomie bevredigende resultate oplewer.
2. Die roetine-prosedure is 'n geen-lis-anastomose agter die kolon.
3. Dreinering deur middel van 'n maagpomp deur roetine-jejunostomie verhoog die gerief van die pasiënt ná die operasie, en dra heelwat daartoe by om die operasie veiliger te maak.
4. Die sterftesyfer ten gevolge van die operasie is laag—1.3% in 154 gevalle, insluitende 'n noodgastrektomie vir onbeheerbare bloeding.

Modern surgery is a matter of team-work. The author is grateful to those who have given such invaluable help in his work, and wishes especially to mention the members of his present team: Dr. N. C. Leiman, Dr. S. Hoffmann and Mr. A. Leonsins. All these cases have been operated on at the Lady Dudley Nursing Home, and he is deeply indebted to the matrons and the staff for their never failing co-operation and nursing skill.

I am grateful to Dr. E. A. Thomas for the drawings.

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CYANOSIS IN INFANCY

ITS INVESTIGATION AND TREATMENT

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Cyanosis indicates oxygen unsaturation, and may either be observed at birth or at any time during the period arbitrarily designated as infancy. A complete history of the birth from the mother or attendant is very important, as this information will direct attention to the system which is at fault.

The presence of cyanosis merely indicates that there is more than 5 g.% of reduced haemoglobin in the circulatory system. It does not necessarily imply that the fault lies in the circulatory system, as abnormality of any of the bodily systems may result in its appearance.

CYANOSIS AT BIRTH

The 2 common causes of neo-natal cyanosis are respiratory centre depression and respiratory tract obstruction. Depression of the infant's respiratory centre, resulting from ill-timed or over-administration of opium derivatives to the mother, is a well known and easily recognized entity. It must be remembered, however, that trauma to the child's head as a result of a prolonged labour or misapplied forceps may produce similar depressant effects from actual damage to the respiratory centre.

Obstruction of the trachea due to a plug of mucus may cause deep cyanosis. This complication may either be prevented or immediately diagnosed and treated, if careful obstetrical care and judgment are exercised.

Cyanosis at birth must always be regarded as a form of asphyxia which, if not relieved, will be fatal.

CYANOSIS AFTER BIRTH

Cyanosis may develop slowly within a few days of birth or may only be evidenced at a later stage of infancy. It may be paroxysmal, the infant appearing quite normal in the intervals between attacks. Paroxyms may be related to crying or to feeding, facts which can readily be elicited by careful questioning. Continuous cyanosis is suggestive of a serious lesion and, if it becomes progressive, the diagnosis and any possible treatment become a matter of urgency. The degree of cyanosis may vary, appearing more marked at some times than at others. These fluctuations in intensity may be related to temperature changes, e.g. the cyanosis may deepen as the infant becomes colder.

History of the Onset. It has already been pointed out that a good history may provide the key to the diagnosis.

Specific questions should be asked of the mother. When did she first notice the cyanosis? It may only have become obvious when the child was several days old. The mother may state that though the child becomes blue when it is being breast fed, it is normal between feeds. This colour change must be distinguished from cyanosis following a feed, which is due to air in the infant's stomach. This history would suggest an obstruction to the trachea by the oesophagus, as occurs in congenital vascular rings of the aorta (Figs. 1 and 2).

Paroxyms of cyanosis with feeding and coughing during the first few days of life suggest the presence of a congenital oesophageal atresia. When the top of the oesophagus fills, it overflows into the trachea, causing the infant to choke. This aspiration of milk and saliva into the lungs may initiate an inflammatory change. The ensuing pneumonia may thus attract attention to the existence of an oesophageal atresia.

Mothers may state that they feel a peculiar purring sensation over the child's chest, or that they hear a purring noise when the child is held close. These mothers may be feeling or hearing cardiac murmurs, and the cardiac abnormality may have been present long before the cyanosis developed. If a congenital cardiac lesion is the cause, the circulatory position may be effective for the very young infant but, as it grows older, the pulmonary circulation becomes inadequate and cyanosis ensues. The amount of cardiac involvement in congenital cyanotic heart disease varies considerably, the severe degrees being incompatible with life.

In late infancy and early childhood the occurrence of cyanosis after a febrile onset should make one suspicious of whooping cough or diphtheria. A history of exposure to these fevers may shed light on the cause of the cyanosis.

A history of paroxyms of cyanosis combined

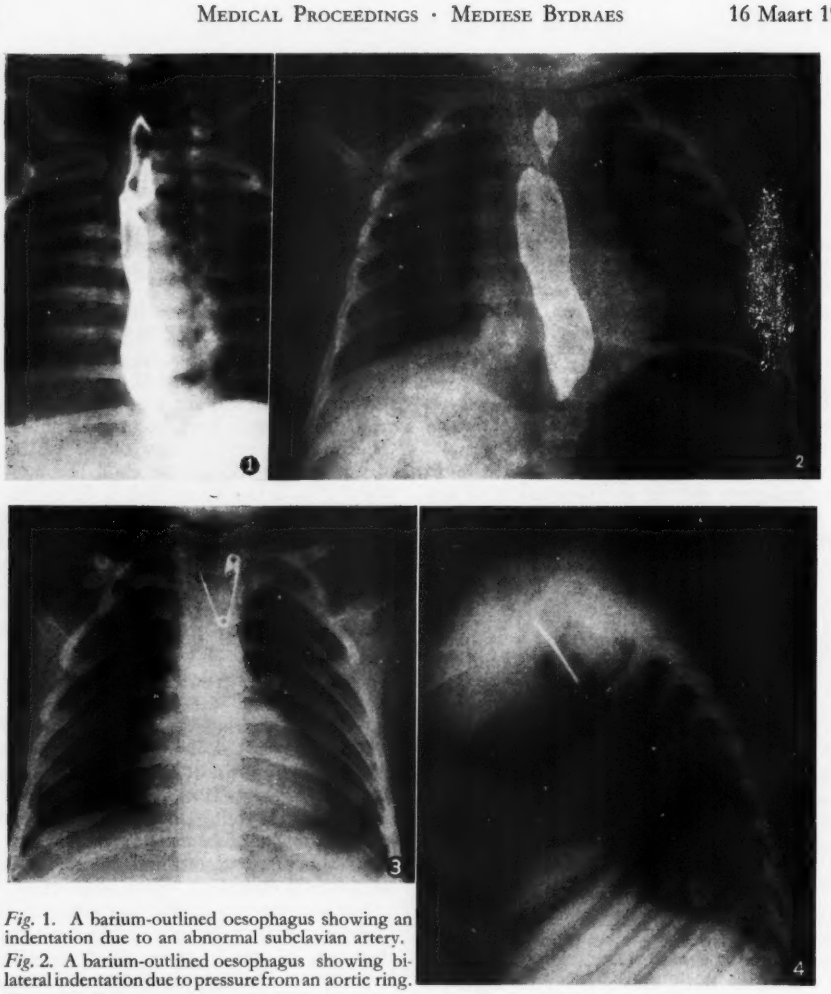


Fig. 1. A barium-outlined oesophagus showing an indentation due to an abnormal subclavian artery.
Fig. 2. A barium-outlined oesophagus showing bilateral indentation due to pressure from an aortic ring.
Fig. 3—4. Postero-anterior and lateral views showing the presence of an open safety-pin in the trachea.

with a bronchial rattle is suggestive of obstruction within the air passages. The aspiration of a foreign body is possible, even in earliest infancy (Figs. 3 and 4).

CLINICAL EXAMINATION

Physical examination may prove of little value. The infant should be exposed completely in a warm room. Attention should be primarily directed towards ascertaining whether mucus or any foreign material is obstructing the airway.

Inspection may only show the presence of the cyanosis. The respiratory rate may be so rapid and shallow that it is impossible to see if recession of the ribs and sternum is present. On the other hand, it may be possible to detect that one side of the chest moves well, or that one side of the chest is bulging and moving poorly. In early infancy one is usually unable to see clubbing, but the presence of other obvious congenital abnormalities may suggest that the cyanosis is caused by an underlying congenital cardiac defect.

Obvious markings on the head due to improperly applied forceps may suggest that the congenital cyanosis is due to injury of the underlying brain tissue.

Palpation may confirm the results of observation. A cardiac thrill may be detected. The presence of cyanosis in the toes and the absence of femoral pulses are suggestive of coarctation of the aorta combined with a persistent ductus arteriosus. The cardiac impulse may be grossly displaced, and its position on palpation will indicate the situation of the heart. The relationship of the mediastinum to the side of the chest evidencing poor movement will show whether it has been displaced from, or pulled towards, the affected side (Fig. 5).

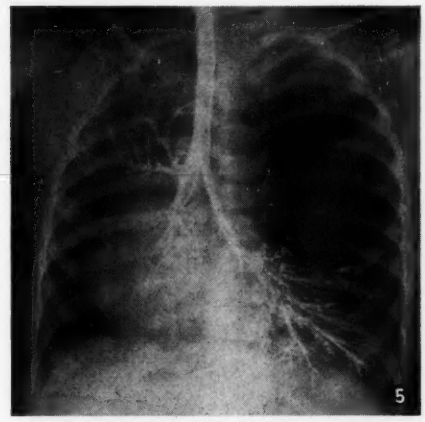
Percussion may show the presence of either a solid or an air-filled pleural cavity, confirming the impression reached by palpation. An infant's chest is so very small that an air-filled stomach may make the entire thorax resonant to percussion. In later infancy, it is quite simple to percuss a collapsed lobe of the lung, or the area of cardiac dullness.

Ausculation may also prove misleading. The rapid respiratory rate may make it almost impossible to distinguish between bronchial breathing and harsh vesicular breath sounds. A unilateral wheeze, absent breath sounds or a distinct area of bronchial breathing may, however, be conclusive evidence of abnormality (Fig 6).

Cardiovascular System. It has already been stated that the examination of an infant should always include an attempt to elicit femoral arterial pulsations.

Routine examination of the heart may reveal cardiac murmurs, but the rapid heart rate may render timing of these murmurs impossible. The murmurs of a persistent ductus arteriosus or a pulmonary stenosis, however, may be quite definite. The importance of determining the presence of a cardiac lesion as the cause of the cyanosis is obvious, as today so much can be done to relieve these infants. In past years, infants were said merely to have congenital cardiac disease, with or without cyanosis, but the exact diagnosis often remained unknown.

The Throat. No examination of a cyanosed child is complete without an inspection of the throat. Note should be taken of signs of infection, oedema of tissues, inflammatory membrane and the presence of hypertrophied lymphatic follicles.



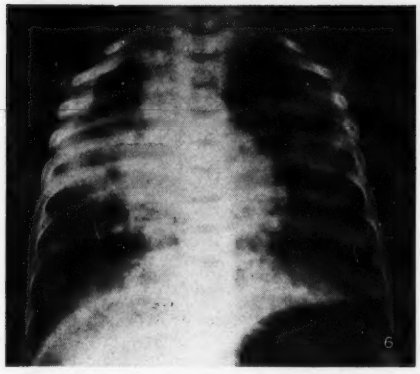


Fig. 5. A tension cyst of the left lung causing displacement of the mediastinum.

Fig. 6. Extensive lung involvement from miliary tuberculosis.

SPECIAL INVESTIGATIONS

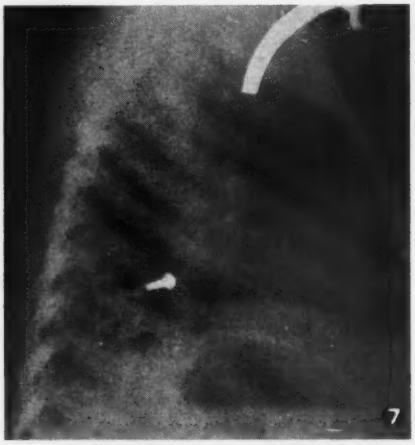
Further investigations may be necessary to localize the affected system, or to determine or confirm the exact nature of a lesion suspected by ordinary methods of examination.

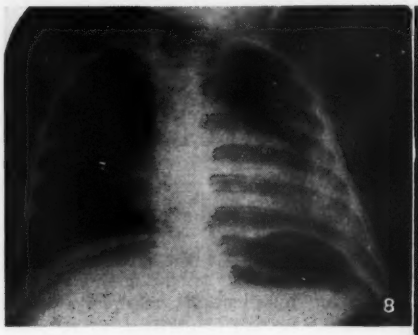
It is very important to know not only the underlying cause of the cyanosis, but also whether any special features are present, e.g. A Fallot's tetralogy may be the cause of cyanosis, but special investigations will be necessary to show the state of the pulmonary arteries, on which the success of an anastomising operation will depend.

X-Ray Examination. The special investigations are, in the main, radiographic. One must always remember that the lung fields are diminutive, because not only is the chest of the infant small, but the respiratory and cardiac rates are very rapid, the heart shadow is disproportionately large, and the abdominal contents squeeze up the diaphragm.

A good quality radiographic film must therefore be one which is exposed for a very short time, e.g. 0.02 second (Fig. 7).

The small size of the infant's chest and the impossibility of taking erect films in earliest infancy, render this examination difficult. Only a small area of lung field is visible when the infant, with its high diaphragm and large heart, lies in the prone position. All the usual and special X-ray examinations must, however, be carried out.





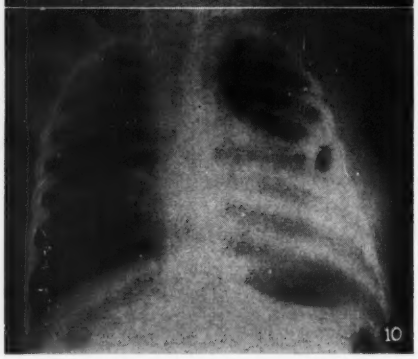


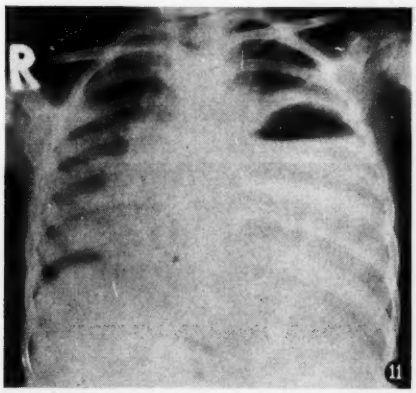
Fig. 7. A foreign body in the lung (a screw) for which a tracheotomy was necessary.
Figs. 8—10. The stages of an empyema necessitans finding its way through the chest wall into the subcutaneous tissues.

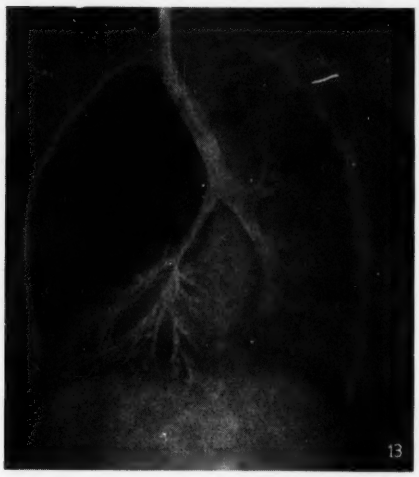
Conventional Radiographs. The conventional views should be taken. A.P. and oblique views will provide the most information, while lateral views are often of great assistance in diagnosis.

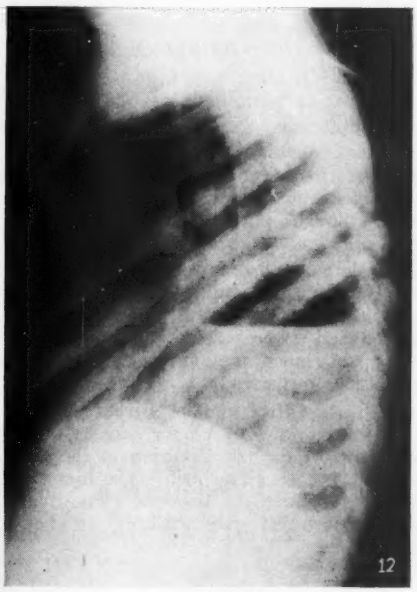
Cyanosis of pulmonary origin results from a reduction in the area of functioning lung tissue. This may be due to compression of one lung by a collection of fluid or air under tension, the same effect being produced by a large tension air cyst. The lung becomes compressed and the mediastinum is displaced to the opposite side. The opposite lung undergoes changes, becoming engorged, and slightly compressed, and in certain cases appears atelectatic. This obviously leads to many diagnostic errors, the lesion being placed on the wrong side, and its nature being incorrectly assessed (Figs. 8-10).

In later infancy, where the cyanosis is caused by the aspiration of a foreign body, difficulty may be encountered in determining the site of the bronchial obstruction, as a partial atelectasis is produced when the bronchus is incompletely occluded. Displacement of the mediastinum towards the affected side results in over-distension of the normal lung tissue.

Such a picture closely resembles that of obstructive emphysema, in which the affected side is over-distended (Figs. 11-13). In such cases, examination of the infant under the







Figs. 11—12. Postero-anterior and lateral views showing an infected cyst of the lung.

Fig. 13. Oblique view showing compression of the lung due to the presence of a large cyst in the left upper zone.

fluorescent screen may be of assistance. In obstructive emphysema, the mediastinum is fixed, though displaced to the opposite side. In partial atelectasis the mediastinum is still able to move on respiration. This observation generally applies, the exception being seen in a case reported by Greenwood and Phillips, in which the obstruction acted like a cork, plugging the bronchus with inspiration.

Assessment of the radiographic examination of the respiratory system must include careful regard to the following features:

(a) The symmetry of the thoracic wall.

(b) The position of the mediastinal structures.

(c) The levels and silhouette of the domes of the diaphragm.

(d) The translucency of the lung fields.

(e) The presence of unusual shadows in the lung fields.

OPSOMMING

Die twee gewone oorsake van sianose by pasgeborenes is 'n depressie van die asemhalingsentrum en 'n obstruksie van die asemhalingskanaal.

Sianose by geboorte moet altyd beskou word as 'n soort asfiksie wat, as dit nie verlig word nie, bes moontlik noodlottige gevolge kan hê.

Sianose kan ook binne 'n paar dae na geboorte stadig ontwikkel, of kan eers op 'n latere stadium van die kleinkinderjare sigbaar word. 'n Sorgvuldige bestudering van die geskiedenis van die geval bied dikwels die sleutel tot diagnose.

Die toestand kan paroxysmaal wees (d.w.s. dit kan in verband staan met huilery of voeding), of dit kan ononderbroke en progressief wees (d.w.s. 'n ernstige hartletsel). Die intensiteit van sianose kan ook wissel—iets wat in verband kan staan met temperatuursveranderings (bv. die sianose kan dieper word namate die suigeling kouer word).

Die verskillende toestande wat sianose tot gevolg kan hê, word in oënskou geneem, en die skrywer beklemtoon die betekenisvolle kenmerke in die kliniese en spesiale ondersoeke wat onderneem moet word by die behandeling van hierdie toestand.

(*To be continued*)

A MEDICAL ATLAS

DERMOLIPOMA OF THE CONJUNCTIVA

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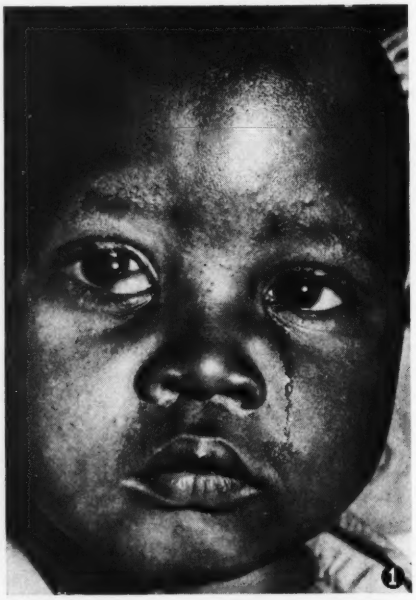
The vast majority of fibro-fatty tumours occurring in the conjunctiva are dermoid in nature, though pure lipomata have been described.

The dermolipoma is a tumour of congenital origin, often multiple and symmetrical and usually found up and out between the superior and external recti. They are also seen at the inner angle in association with the plica or caruncle.

Fig. 1 shows the pre-operative picture of an African child with a large tumour of the conjunctiva of the nasal portion of the right lower lid, present since birth. The lump was excised to remove the cosmetic blemish and was demonstrated pathologically to be a dermolipoma.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OPSOMMING

Die groot gewas van die oogbindvlies van die neusgedeelte van die onderste ooglid aan die regterkant, soos geïllustreer in Fig. 1, was aanwesig sedert geboorte.

Die klont is chirurgies verwyder, en het geblyk 'n dermolipoma te wees.

CALCIFIED INTRACRANIAL TUBERCULOMA

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Tuberculomata of the brain are rarely encountered and constitute 1-3% of brain tumours[1]; 50% are observed in children in the first decade and multiple lesions are more frequent than solitary ones, appearing as often in the cerebrum as in the cerebellum.[2]

Calcification in intracranial tuberculomata is most uncommon. Evans and Courville[2] maintain that it occurs in 6%, but Lorber[3] states that probably less than 1% of true cases of tuberculoma show calcification. Nevertheless, tuberculosis is likely to be an increasingly common cause of intracranial calcification in future years, because large numbers of cases of tuberculous meningitis are being treated and cured by antibiotics.[4] Lorber,[3] Garsche[5] and Russel and MacArthur[6] have shown that calcification occurs in the basal exudate of an appreciable proportion of these cured cases. No calcification was detected in any patient in less than 18 months from the beginning of treatment.

The following case is notable in that calcification occurred in a proved tuberculoma, and also because after anti-tuberculous treatment further extensive calcification occurred in 13 months.

CASE REPORT

J. T., a 14-year-old Bantu female, was first admitted to Baragwanath Hospital on 31 August 1955, complaining of cramp in the left

foot and hand for 2 months. She woke up to find that her left leg was weak and numb and a few days later her left foot was similarly involved.

She had had headaches for some years, especially at night, and a fit on one occasion. She complained also of a discharging right ear.

Examination. Bilateral papilloedema and a left homonymous hemianopia were found.

Left upper motor neurone hemiparesis was present.

The right ear showed chronic otitis media.

INVESTIGATIONS

The blood count was normal.

Lumbar puncture revealed a pressure of 180 mm. of water. There was no block.

The cell count was 4 lymphocytes per c.mm.

Total protein, 60 mg. per 100 c.c.

Chlorides, 721 mg. per 100 c.c.

Sugar, 40 mg. per 100 c.c.

Fig. 1 is an X-ray of the skull taken on 11 September 1955. It shows fairly well-defined rounded opacity (3 cm. × 3 cm.) in the right occipito-parietal area of the skull, consisting of patchy calcification. A smaller area of calcification is present behind the right mastoid area, which shows loss of cell outline and sclerosis. Marked widening of the sutures is present, indicating increased intracranial pressure.

An X-ray film of the chest showed the lungs to be clear.

A right carotid angiogram revealed a shift of the anterior cerebral artery to the left.

The most likely diagnosis was either a cerebral abscess following chronic mastoiditis, or a tuberculoma. In view of the increased intracranial pressure it was decided to explore the skull through burr holes.

A small burr hole was made and caseous material was found. Section of the tissue reported on by Dr. R. V. Dando, of the South African Institute for Medical Research, showed 'small irregular fragments of chronic granulation tissue and necrotic caseous material. Although no acid-fast bacilli were observed in the section examined, the histological features suggest tuberculosis'.

Treatment. The patient was put on streptomycin 1 g. daily and I.N.H. 100 mg. *t.d.s.* for 1 month, and then Streptomycin 0.5 g. daily for 3 months. Crysticillin was given for her ear condition.

Progress. The patient was seen on 10 December 1955, when she said she felt very much better. She was given Rimifon 100 mg. *t.d.s.*

She was seen again in September 1956. The left hemiparesis was still present but much improved. The papilloedema and hemianopia had disappeared.

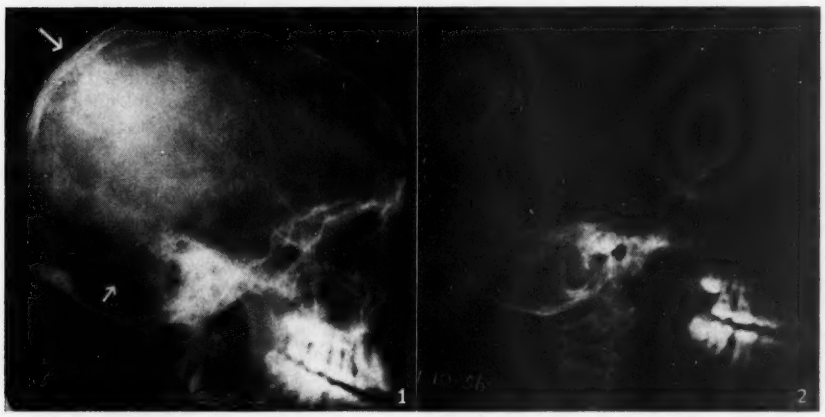

Fig. 1. Lateral view of the skull taken on 6 September 1955, showing the areas of calcification (indicated by the arrows).

Fig. 2. X-ray taken 13 months later (11 October 1956) showing the great increase in calcification, which now involves most of the right occipital region.

The cerebrospinal fluid pressure and constituents were now within normal limits. The total protein was 25 mg. per 100 c.c.

An X-ray of the skull on 11 October 1956 showed much more extensive calcification than was revealed in the previous film of 11 September 1955. The calcification involved most of the right occipital region and there were no signs of suture widening (Fig. 2).

DISCUSSION

The actual mechanism of calcium deposition is uncertain. Evans and Courville[2] consider that it may result from fatty acids in the decadent tissues, impaired tissue respiration, or favoured by hyalinization of the adjacent connective tissue. Access to the circulation is essential. They state that pathologically tuberculoma of the brain contains 3 distinct zones. The centre has a structureless caseous core, the outer zone has hyalinized connective tissue, and at the junction calcification may occur. This layer usually becomes indented and fractured as the outer zone of connective tissue shrinks and the necrotic centre of the tuberculoma is absorbed or calcified.

On the basis of this pathology Weinberger and Grant[7] analyzed the literature and observed that the calcareous deposits in tuberculoma of the brain often cast a characteristic shadow on X-ray, i.e. calcification is homogenous in the centre, but there is a serrated, lace-like, angular margin representing the intermediate calcified zone of the tuberculoma. In those lesions in which the indentation and fragmentation of the calcareous shell are more pronounced, small calcium spicules and plaques are seen to be separated from the main centre of calcification. However, Sutton[4] maintains that a diagnosis can never confidently be made on radiological grounds, because calcification in intracranial tuberculoma is so rare. In the few cases of proved tuberculoma he has seen, none showed radiologically demonstrable calcification. He thinks that the diagnosis has been made far too readily on the basis of a focal neurological lesion occurring in a patient with pulmonary tuberculosis, particularly if a calcified intracranial lesion is demonstrable on X-ray.

The calcification in the brain following tuberculous meningitis may follow 4 possible causes.[3] It may be due to calcification in:

i. Areas of healed tuberculous encephalitis;

ii. Areas of encephalomalacia following cerebral infarction;

iii. Tuberculous exudate in the meninges; or

iv. It may represent a calcified intracranial tuberculoma.

Anti-tuberculous drugs, especially Streptomycin, are important factors in causing rapid calcification because of the bacteriostatic property of the drug which is indirectly responsible for causing fibrosis.[8] However, Cushing[9] observed the appearance of calcification in two cases of intracranial tuberculomata which had been treated by decompression only and not removed. In our case there were both factors of decompression and antibiotic therapy, and this may have accounted for the rapid development of the calcification.

SUMMARY

A case of calcified intracranial tuberculoma is described.

The pathology, radiological diagnosis and the possible mechanism of calcification in the brain are discussed, as well as the factors influencing the rate of calcification.

I should like to thank Dr. V. H. Wilson for allowing me to have access to the notes on this patient (who was under his care) and to the Superintendent of Baragwanath Hospital for permission to submit this case for publication. I am grateful to Mr. Shewitz of the Department of Medicine for help with the photographs.

OPSOMMING

'n Geval van verkalkte binneskedel-tuberkuloma word beskryf.

Die patologie, radiologiese diagnose en die moontlike meganisme van verkalking in die brein word bespreek, sowel as die faktore wat die tempo van verkalking beïnvloed.

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CARCINOMA OF THE LUNG

ITS DIAGNOSIS

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The diagnosis of carcinoma of the lung is a challenge. Deaths due to carcinoma of the lung have increased 40 times in 40 years. In 1916 to 1920 there were 428 deaths per annum in England; in 1954 there were 16,331. (A. McKenzie, Brit. Med. J., 20 July 1956). The present position is that of 100 patients with bronchial carcinoma, 70 to 80 will be dead within a year of diagnosis, and only 10 will be alive at the end of five years. This is an appalling state of affairs. It is mainly due to two reasons. First, in most cases the disease has spread too far by the time a diagnosis has been made. Secondly, many patients are unable to stand radical therapy for one or another reason, and the best that can be done is to offer palliative treatment.

A generation ago the early diagnosis of carcinoma of the lung was a matter of comparatively little importance, since treatment was entirely symptomatic. To-day, however, a very real responsibility rests on the physician and the general practitioner, for early diagnosis makes all the difference in the effectiveness of treatment, and the methods to be adopted.

The first thing for all of us is to have the condition constantly in mind, for the manner of presentation may vary tremendously.

The most common way in which it presents itself is by way of cough and haemoptysis. When these symptoms occur in a patient over the age of 40, a carcinoma of the lung should be presumed to be present until it is proved to be otherwise. The common acceptance of the cough being 'only a smokers' cough' is frequently a cause of fatal delay. The prolonged use of cough mixtures, instead of adequate investigation, may be equally fatal.

The history of repeated attacks of pneumonic illnesses should immediately awaken suspicion, the presence of anomalous physical signs in a pneumonic-like illness, or the unusual course of a pneumonic illness with failure of resolution should also make us suspect a carcinoma.

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An haemoptysis should never be passed over as being due to 'rupture of a vein' due to coughing. Immediate investigation is obligatory, and differentiation from tuberculosis is necessary.

Other symptoms are largely due to pressure from the growth itself or from secondary deposits. Collapse of a lobe of the lung may follow, causing paroxysmal cough; or hoarseness of the voice may indicate a paralysis of the recurrent laryngeal nerve. Less commonly the phrenic nerve may be pressed upon with palsy of one side of the diaphragm.

The superior vena cava may be pressed upon with enlargement of the veins of the head and neck and oedema, while veins of the chest wall may show secondary dilatation.

A pleural effusion, especially if it is blood-stained, in a patient over 40, may be the first indication of malignant disease of the lung, while under 40 it is more likely to be due to tuberculosis. The rapid development of clubbing of the fingers and toes may be the first hint of a pulmonary neoplasm.

All these symptoms and signs may be associated with undue dyspnoea, which is not due to cardiac disease or anaemia, and while the patient's general condition is surprisingly good.

I have also seen two cases in the last few years which presented as dyspepsia, where there was no disease of the gastro-intestinal tract.

The usual method of spread of a carcinoma of a bronchus is to the broncho-pulmonary glands, then to the mediastinum and finally to extra-thoracic sites. Presenting symptoms may be due to involvement of the latter, while the primary growth remains inconspicuous. Metastases in the brain are not infrequent, and the case presents as a neurological problem. The case may present with a liver enlargement due to metastases and, less to be expected, the suprarenals may be involved. This last was one of the most common sites for metastases found in a series of 272 cases described by Oswald (Brit. Med. J., 7 April 1956).

Even less expected was the finding of Brain in 1951 (J. Neurol. Neurosurg., 14, 59) that

a cerebellar degeneration occurred in some cases of bronchial carcinoma apart altogether from any question of metastases, the cases presenting as such.

Further, it is well known now that cases may present with peripheral neuritis or signs of a myopathy, and to conclude the neurological presentations, Charatan and Breirly (Brit. Med. J., 7 April 1956) report 3 cases of proved bronchial carcinoma, presenting as cases of severe toxic confusional psychosis with lucid intervals, and without other neurological signs.

In these cases cerebral or meningeal metastases were absent, but, in all 3, liver metastases were present. It is, however, stated that psychiatric disturbances can occur without such liver involvement. It has been suggested that a pulmonary neoplasm may cause these neurological symptoms by, in some manner, causing an avitaminosis (Denny-Brown, J. Neurol. Neurosurg. 1948, 11, 73).

Be that as it may, our main task at present is to appreciate the many and varied ways in which these cases can present. Once the suspicion arises that a pulmonary neoplasm may be present, special investigations are undertaken. First a skiagram of the chest is taken, and the E.S.R. is estimated. Then bronchoscopy is carried out. This is the most important investigation, after radiological evidence; it gives confirmatory evidence in about 60% of cases. It is claimed, however, that in the hands of experts, examination of the sputum for neoplastic cells yields even greater confirmatory evidence. Examination of the sputum is especially useful in investigating peripheral radiological shadows, beyond the reach of the bronchoscope.

Biopsy of extra-thoracic sites of spread, e.g. glands in the neck or axilla, not infrequently clinches the diagnosis. Such sites must always be diligently searched for. Any pleural effusion must be examined microscopically for neoplastic cells. The next step in diagnosis is the determination of the type of cell in the neoplasm.

Three varieties are found: squamous, adenoid and anaplastic. The importance of this is that the more highly differentiated, as the squamous and adenoid, carry a better prognosis than the anaplastic or differentiated type.

Squamous carcinoma often occurs in the main bronchi; while adenocarcinoma tends to be found more at the periphery.

The site of the growth is also of significance, since a growth within one inch of the bifurcation of the trachea is not amenable to surgical treatment, the bronchial stump being so short that the bronchus cannot be closed.

On the other hand, the significance of a peripheral shadow may be very difficult to determine, it being beyond the reach of the bronchoscope, and doubt may remain about its nature until thoracotomy is undertaken.

Quite unlike other carcinomata of the lung, the symptomatology of superior sulcus (Pancoast) tumours deserves separate mention. It is suspected that they arise from bronchial cleft remains, and they occur in the upper part of the lung. Pain in the shoulder and chest is the outstanding symptom, with cough, loss of weight, and a Horner's syndrome. They may grow to a considerable size, and displace the mediastinum to the other side. By the time they are seen the pleura and chest wall are usually involved, so that they are not amenable to surgical treatment, and they do not respond to deep X-ray treatment.

On the other hand, a sarcoma of the mediastinum responds in the first instance very well to radiotherapy.

The main symptom of endotheliomata of the pleura is usually dyspnoea, associated with a pleural effusion, often blood-stained. It is considered by some that they are really secondary deposits from a peripheral columnar-celled carcinoma, which is so small as to escape notice.

The presence of secondary deposits in the lungs is usually fairly easily determined radiologically, but they may have to be differentiated from Boeck's sarcoidosis, miliary tuberculosis, and pneumokoniosis.

Non-malignant tumours, papillomata and adenomata, occur usually in younger people. They do not metastasize, but may be locally malignant, causing haemoptysis and collapse of a lobe or lobes. Diagnosis can only be made by biopsy.

The presence of the more usual primary bronchial carcinoma is suspected by an appreciation of the various presenting symptoms. We prove the presence of a growth and its site radiologically and by bronchoscopy. We determine the nature of the growth either by biopsy or by finding neoplastic cells in the sputum.

But our diagnosis is not complete, for we still have to estimate the condition of the patient. Most post-operative deaths now-a-days are due to complicating pulmonary factors such as emphysema, anoxia, bronchopneumonia; venous thrombosis and embolism, or cardiac conditions such as coronary thrombosis or cardiac failure.

It is here that clinical judgment about the physique and will-power of the patient is of supreme importance, and the question to be answered is: will he stand the major procedure of pneumonectomy?

We are now in a position to divide our patients into 3 groups:

1. Those who are suitable for radical therapy. The best chance we can give a patient is to offer him a pneumonectomy. This applies only to those in whom the growth is resectable, and who, we consider, can stand the operation.

Amongst these the operative mortality is about 10% and the survival rate for squamous or adenocarcinoma, confined to the lung, is about 50% at 5 years.

If for any reason pneumonectomy is not possible, the only other radical treatment is radiotherapy, in which the survival rate is about 3% at 5 years. This poor result may be in part due to the fact that most of those in the most favourable group are usually treated surgically. A limited number of early cases may be helped by lobectomy.

2. The second group consists of those who are generally fit and are capable of working, but who are found to be unsuitable for radical therapy. It may be that there is a suspicious spread to the hilum, or to the glands above the clavicle, or merely that a blood-stained pleural effusion is found. Many of these patients may enjoy 6 months to a year of comparatively good health in ignorance of their condition before going rapidly down-hill, whereas a serious operation, in an attempt to effect a radical cure, may make them unhappy invalids.

The final decision about operation must rest with the thoracic surgeon.

3. The third group consists of those for whom only symptomatic treatment is possible. This consists of palliative radiotherapy, pleural aspiration and the injection of 'mustine' into the pleural cavity, and analgesics. Radiotherapy is most likely to help those whose symptoms are caused by pressure effects, recurrent haemoptyses, persistent cough and metastases in bone.

As regards analgesics, all from A.P. Codein to nepenthe, heroin, morphine and the Brompton cocktail (morphine, cocaine and gin) may be necessary.

It is always a difficult question to decide whether a patient in this group should be told the nature of his complaint. The best approach usually is not to do so, but to confide in the relatives of the patient.

And so we come back to the challenge before us.

Are we content to allow the present appalling state of affairs to continue, or are we, by earlier diagnosis, going to enable more of our patients to benefit by the radical therapeutic means at our disposal?

SUMMARY

The author reviews the differential diagnosis of carcinoma of the lung and classifies patients with this disease into three groups:

i. Those suitable for radical treatment, e.g. pneumonectomy;

ii. Those unsuitable for radical treatment because a serious operation, in an attempt to effect a radical cure, may make them unhappy invalids;

iii. Those for whom only symptomatic treatment is possible.

The author urges that earlier diagnosis will enable more patients to benefit from the radical therapeutic means at our disposal.

OPSOMMING

Die skrywer verstrek 'n oorsig van die differensiële diagnose van karsinoom van die long, en klassifiseer pasiënte wat aan hierdie siekte ly in drie groepe:

i. Dié wat radikale behandeling, bv. pneumonektomie kan ondergaan;

ii. Dié vir wie radikale behandeling nie raadsaam is nie omdat 'n ernstige operasie, in 'n poging om 'n radikale genesing teweeg te bring, hulle bes moontlik ongelukkige invalides kan maak;

iii. Dié wat alleen aan simptomatiese behandeling onderwerp kan word.

Die skrywer meen dat vroeë diagnose meer pasiënte in staat sal stel om voordeel te trek uit die radikale terapeutiese middele wat tans tot ons beskikking is.

THE TREATMENT OF CARDIAC ARRHYTHMIAS

EXPERIENCES WITH AMBONESTYL (2-DIETHYLAMINOETHYLISONICOTINAMIDE HYDROCHLORIDE)

PRELIMINARY REPORT

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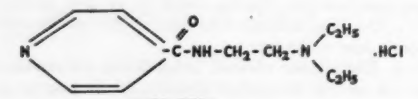
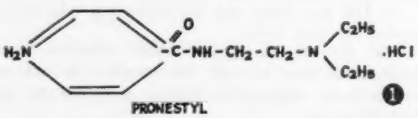
Procaine amide hydrochloride (Pronestyl) has now been used extensively and successfully in the treatment of ventricular ectopic beats and paroxysmal ventricular tachycardia. When given intravenously, however, this drug tends to cause hypotension and an impairment of intraventricular conduction. Many patients with ventricular tachycardia have already developed a falling blood pressure, either due to the tachycardia or to the cause of the arrhythmia, which is often acute myocardial infarction. Furthermore, it may be impossible to distinguish supraventricular paroxysmal tachycardia associated with bundle branch block from ventricular tachycardia. It is in such cases that Pronestyl may prove dangerous.

A further potential hazard exists when 2 : 1 auricular flutter is associated with bundle branch block. Not only may the intraventricular conduction be further impaired, but the atrio-ventricular block may be depressed, giving rise to a 1 : 1 ventricular response. This abrupt doubling of ventricular speed may prove lethal. With quinidine therapy the pitfalls and hazards are similar.

Ambonestyl (2-diethylaminoethylisonicotinamide hydrochloride, M.C. 4112) is a derivative of isonicotinamide synthesized by the Squibb Institute for Medical Research. The empirical formula is $C_{12}H_{19}N_3O.HCl$. The structural formula and its relation to Pronestyl are shown in Fig. 1.



AMBONESTYL



PRONESTYL

Fig. 1

Ambonestyl is a white powder soluble to more than 10% in water, and hydrolytic studies indicate that it is completely stable in solution. Experimental evidence and limited clinical studies have indicated that Ambonestyl is as effective as Pronestyl in suppressing ventricular ectopic rhythms, but has the advantage of greater safety.[1, 2]

Methods and Material. The drug was used intravenously and undiluted as a 10% solution. Injections were always given rapidly. Small doses (e.g. 250 mg.) were administered within 3-5 seconds. Larger doses (0.5-1 g.) were given over periods of 5-10 seconds.

RESULTS

Case 1. An obese female aged 57 years was admitted with a history of effort dyspnoea, angina pectoris and oedema of the feet for 16 months. Three days before admission there was a sudden exacerbation of dyspnoea, and for 12 hours the patient had experienced a continuous dull pain, suggesting myocardial infarction. The patient had been a known hypertensive for 2 years, and was on a maintenance dose of digitalis and a regime for congestive cardiac failure.

Positive features on examination were marked exogenous obesity; blood pressure 160/100 mm. Hg; heart rate 72 per minute with sinus rhythm; slight peripheral cyanosis; orthopnoea; crepitations over most of the lung fields; jugular venous pressure + 3 cm. at 60°; 4-finger tender hepatomegaly; marked ankle and moderate sacral oedema. The heart could not be palpated and heart sounds were difficult to assess because of dyspnoea and obesity.

The patient was treated for congestive failure and acute cardiac infarction. Forty-eight hours later she appeared to be in combined forward and backward failure and was obviously deteriorating. The blood pressure had dropped from 160/100 to 115/70 mm. Hg and the heart rate was slightly irregular

at approximately 175 per minute. The history suggested that an attack of paroxysmal tachycardia had commenced some 15 hours earlier.

The electrocardiogram at this stage suggested paroxysmal ventricular tachycardia with dropped beats, although it was impossible to exclude a supraventricular paroxysmal tachycardia associated with left bundle branch block and dropped beats.

Two doses of 250 mg. each of a 10% solution of Ambonestyl were given by intravenous injection at 4-minute intervals. Both injections were given within 3-5 seconds. Immediately after the second injection the paroxysm ended abruptly, and the heart rate dropped from 175 to 80 per minute. At this stage the blood pressure was being recorded at one minute intervals and both systolic and diastolic levels actually increased and continued to do so for one hour. After this the pressure gradually dropped and stabilized at about 100/75 mm. Hg.

The patient complained of a sensation of warmth in the face immediately after the first injection. This was trivial and subsided completely in less than one minute. No skin discoloration was observed.

No prolongation of the QRS complexes occurred, nor did the R and S waves alter significantly. The T waves were reduced in size, but this was assumed to be due to the abolition of summation and this was subsequently confirmed by comparison with earlier

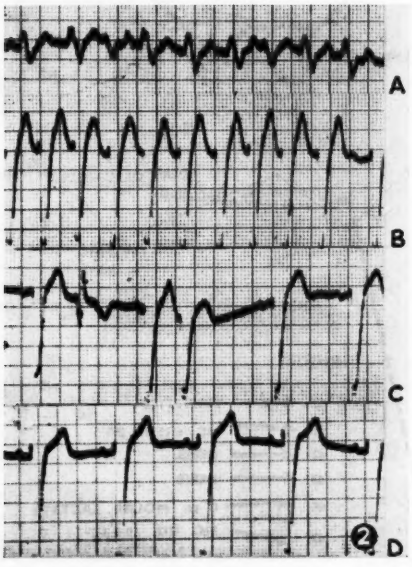
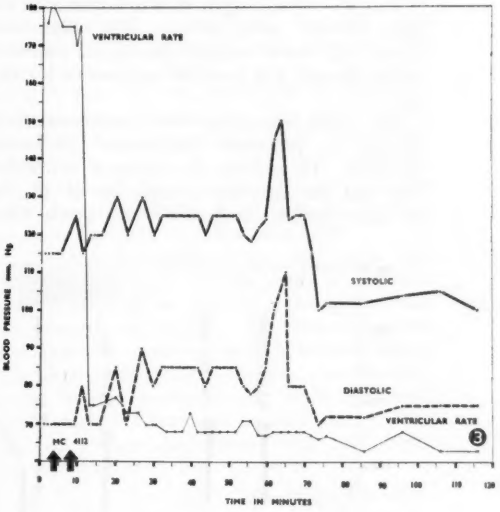


Fig. 2. Case 1.
A: Standard lead II before Ambonestyl.
B: Lead VI before Abonestyl.
C: Lead VI immediately after the second 250 mg. dose of Ambonestyl and 4 minutes after the first 250 mg. dose, showing abrupt cessation of the attack.
D: Lead VI 30 minutes after the cessation of the attack.



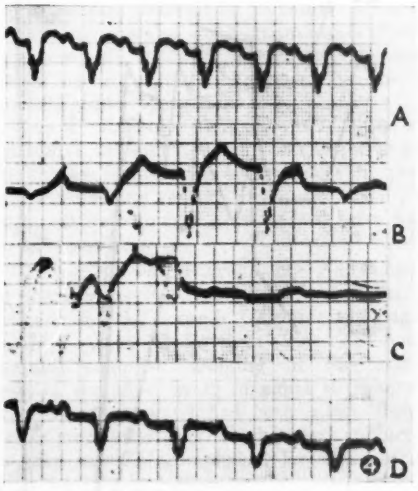


Fig. 4. Case 2.
A: Preoperative standard lead II.
B: Ventricular irritability during aortic valvotomy.
C: Onset of ventricular fibrillation.
D: 30 minutes later.

and later records that were obtained.

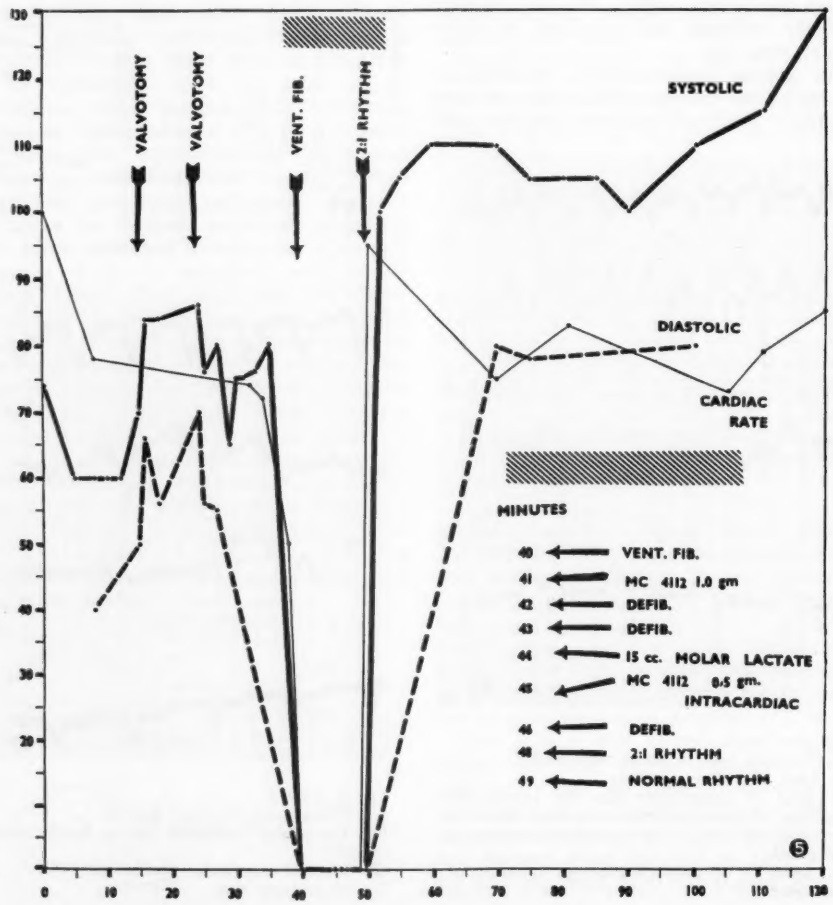
In retrospect, it seemed as if the attack was a supraventricular paroxysmal tachycardia arising near the atrio-ventricular node and associated with dropped beats and permanent left bundle branch block.

The results after Ambonestyl are summarized in Figs. 2 and 3.

Case 2. A male aged 45 was admitted with tight valvular aortic stenosis, left ventricular failure and severe angina. Associated coronary atherosclerosis was partially responsible for the pain.

An aortic valvotomy was performed and during the procedure ventricular fibrillation occurred. In addition to electrical defibrillation and the intravenous injection of 15 c.c. of molar lactate, Ambonestyl was given. One gramme was injected intravenously within 5-10 seconds. This was followed 4 minutes later by 0.5 g. into the cavity of the left ventricle. Four minutes later, after a period of 2:1 rhythm lasting approximately one minute, normal cardiac contractions returned, and the blood pressure increased rapidly. No significant alteration in the QRS complexes or the individual components occurred, but the PR interval, previously 0.26 second, had increased to 0.32 second. This returned to the pre-operative figure of 0.26 second 5 hours later and may well have been due to other factors, such as hypoxia, rather than to the Ambonestyl. The patient made a complete recovery from this episode and was eventually discharged from hospital.

The results are summarized in Figs. 4 and 5.



Case 3. An emaciated male aged 78 was admitted with advanced chronic hypertrophic emphysema, bronchial asthma, acute bronchopneumonia and early cor pulmonale. Gradual improvement occurred until the seventeenth day, when he suddenly collapsed. No history was possible, for the patient was stuporose.

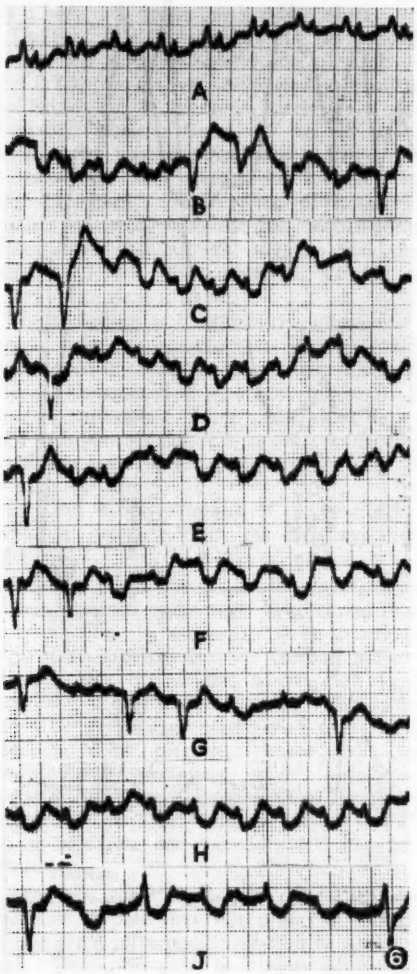


Fig. 6. Case 3.
A: Lead II after onset of collapse.
B: Immediately before Ambonestyl.
C: One minute later, immediately after 0.5 g. Ambonestyl.
D: 15 minutes later, immediately after 0.5 g. Ambonestyl.
E: 3 minutes later, immediately after 0.25 g. Ambonestyl.
F: 6 minutes later; 0.25 g. Ambonestyl given.
G: 25 minutes later.
H: 10 minutes later, immediately after 1 g. Ambonestyl.
J: 17 minutes later.

The salient features on examination were stupor, severe acute pulmonary oedema, heart rate of approximately 150 per minute with sinus rhythm, and a jugular venous pressure of + 2 cm. at 30°. The entire venous level was increased. Peripheral cyanosis was marked and the limbs and nose were cold and clammy. The blood pressure, previously 135/80 mm. Hg, was perceptible by palpation only, at about 50 mm. Hg. The electrocardiogram at this stage revealed sinus tachycardia, large right atrial P waves and ischaemic depression of the ST segments and T waves over the left ventricle. A provisional diagnosis of acute coronary occlusion was made.

The patient rapidly went into coma and developed unequal pupils with a positive plantar response on one side. He appeared to be terminating rapidly. He was digitalized intravenously without any beneficial effect. The ischaemic changes on the electrocardiogram became profound and were associated with marked ventricular irritability. It was decided to use Ambonestyl, and the results are summarized in Figs. 6 and 7.

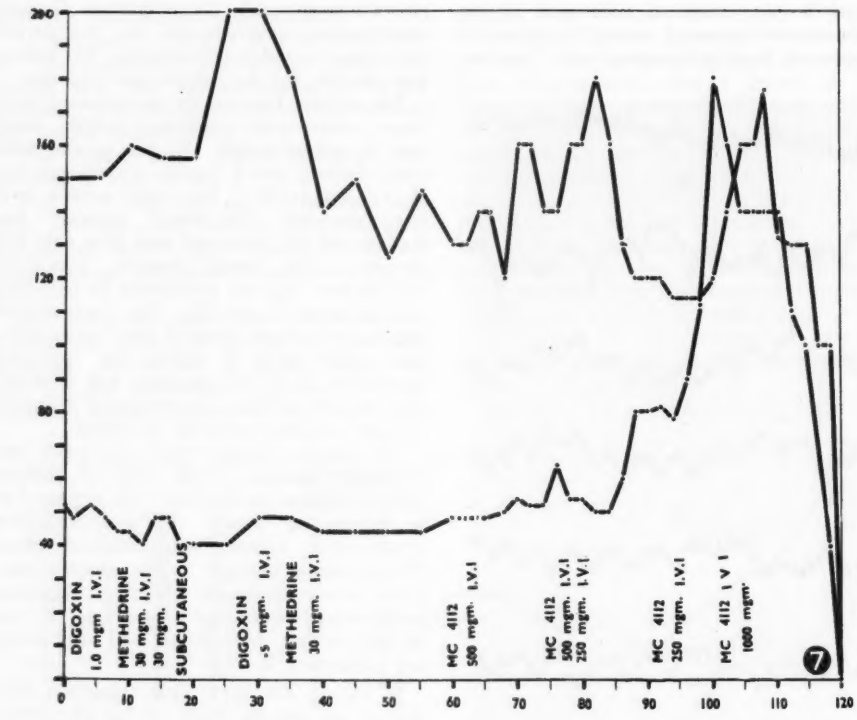
In Fig. 7 the upper line represents ventricular rate and the lower tracing the systolic blood pressure obtained by palpation.

Necropsy revealed complete occlusion of the right coronary artery by ante-mortem haemorrhage one inch from the orifice. No major cerebral lesion was present.

Case 4. A female aged 62 was admitted in congestive cardiac failure of obscure etiology. A striking feature was the presence of persistent multifocal ventricular and nodal ectopic beats. Approximately 1 in every 4 beats was an extrasystole.

The patient was given 250 mg. Ambonestyl by intravenous injection, the injection being given within 3-5 seconds. Electrocardiograms recorded every 2 minutes for one hour revealed complete damping of the extrasystoles, the effect being maximal 30 minutes after the Ambonestyl had been given. Fifty-five minutes after injection the effect appeared to have subsided completely, for the ectopic beats were again frequent.

An apparent slight drop in the systolic blood pressure was almost certainly due to relief of anxiety, for the blood pressure dropped to the patient's usual levels, and daily recordings after this were similar. The only



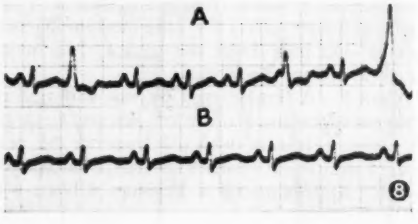
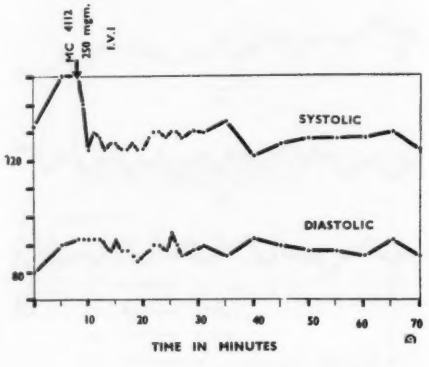


Fig. 8. Case 4.
A: Standard lead II before Ambonestyl.
B: After 250 mg. dose of Ambonestyl.



subjective sensations complained of were a feeling of warmth in the face and a bad taste in the mouth. These occurred immediately after the injection had ended, were trivial, and subsided within about 30 seconds. Trivial flattening of the T waves was noted and thought to be due to Ambonestyl, but subsequent tracings suggested this to be within normal limits of variation for this patient. The results of this case are summarized in Figs. 8 and 9.

The patient was then given Quinidine Sulphate orally gr. 3 six-hourly, but this failed to make any impression on the ectopic beats. Larger doses could not be tolerated because of nausea. Pronestyl in doses of 250 mg. 4-hourly caused only partial damping of the extrasystoles, but 500 mg. 6-hourly orally appeared to have the same effect as the Ambonestyl.

DISCUSSION

Despite the small series, it is obvious that Ambonestyl, when administered intravenously, has a very definite anti-arrhythmic effect.

The paroxysmal tachycardia in Case 1 ended immediately after the second dose of Ambonestyl. The patient who developed ventricular fibrillation during surgery received 3 defibrillating electric shocks, 15 c.c. of molar lactate and 1.5 g. of Ambonestyl. Any or all of these may have caused the reversion to normal rhythm. A time lag of nearly 3 minutes followed upon the last defibrillating current, and this strongly suggests that the Ambonestyl was responsible for causing a reversion to sinus rhythm.

The moribund state and later autopsy findings in Case 3 suggested that no drug could have helped this patient. This patient received 2.50 g. Ambonestyl in one hour, given in 5 separate injections. After every dose, however, temporary suppression of ventricular irritability occurred for periods of as long as 25 minutes (Fig. 6).

In Case 4 the suppression of ventricular and nodal extrasystoles by the drug was very definite.

A distinct disadvantage in the use of intravenous Pronestyl is the acute hypotension that occurs.[3, 7] This hypotension may be hazardous in patients with coronary or cerebral atherosclerosis, and in subjects where the blood pressure is already unduly low. It is also probable that in patients accustomed to a high systemic blood pressure, similar falls in pressure may precipitate major thrombotic episodes. Pronestyl hypotension, therefore, necessitates that the drug be given slowly, usually at a rate not exceeding 100 mg. per minute.

From the cases studied in this series, no significant hypotension was observed following the rapid intravenous injection of Ambonestyl. This, obviously, is a great advantage. In Case 3 the concomitant use of Methidrine, and the difficulty in measuring the pressure, make assessment of possible hypotension difficult, but close analysis suggests that no such hypotension occurred. Clark and Etsten,[1] reporting on a series of 8 unanaesthetized patients and 8 additional cases, concluded that the intravenous injection of Ambonestyl caused only slight, brief hypotension. Extensive laboratory studies[2] confirm the absence of significant hypotension and suggest that this is due to the fact that Ambonestyl exhibits only one-third of the ganglion-blocking activity of procaine amide.

Procaine amide may depress cardiac conduction sufficiently to limit its use in certain patients, especially those with conduction disturbances such as bundle branch block.[4] This assumes particular importance because of the not infrequent case where a supraventricular paroxysmal tachycardia with associated bundle branch block cannot be differentiated from a true ventricular tachycardia.

In this series no significant effect on intraventricular conduction was noted. Case 1, with established bundle branch block, actually received 0.5 g. Ambonestyl intravenously without any detrimental effect on conduction. In the patient subjected to aortic valvotomy, the PR interval changed from 0.26 second before surgery (and Ambonestyl) to 0.32 second after the drug had been given; but because of the hypoxia and mechanical trauma during ventricular fibrillation, and as the PR interval took 5 hours to return to the pre-operative level, it would seem most unlikely that the Ambonestyl was the causal agent.

The conduction disadvantages of procaine amide may also occur with quinidine therapy.[5] The oral treatment of arrhythmias with quinidine may be too slow for urgent cases. The hypotensive action of quinidine is also a serious limitation in cases in which intravenous administration may be indicated.[6]

These preliminary results suggest that Ambonestyl has distinct advantages over procaine amide and quinidine in the treatment of certain cardiac arrhythmias, more particularly those of ventricular origin, and in patients where it is desirable to avoid producing or aggravating systemic hypotension.

The apparent absence of depression of cardiac conduction is also a very important consideration.

That large doses of Ambonestyl can be administered rapidly by the intravenous route also suggests that this drug may supersede both quinidine and procaine amide in a large number of cardiac patients.

SUMMARY AND CONCLUSIONS

1. Ambonestyl, when injected intravenously, appears to be a powerful anti-arrhythmic agent.

2. Large doses of the drug were given rapidly without causing significant hypotension or depression of cardiac conduction.

3. These results suggest that Ambonestyl has

distinct advantages over both procaine amide and quinidine.

OPSOMMING

1. Dit skyn asof Ambonestyl wat binne-aars ingespuit word, 'n kragtige anti-aritmiese middel is.
2. Groot dosisse van die middel is vinnig toegedien sonder dat dit betekenisvolle hipotensie of depressie van die hartgeleiding veroorsaak het.
3. Die resultate dui daarop dat Ambonestyl besliste voordele bied in vergelyking met prokaïenamied en chinidien.

I am indebted to Squibb International Division, New York, and their Johannesburg agents, Protea Pharmaceuticals Ltd., for supplying the Ambonestyl-Squibb used in this investigation; to Prof. G. A. Elliott for his co-operation and encouragement; Dr. M. McGregor for useful criticisms; Dr. B. Ordman for referring Case 1 and Mr. David Adler who performed the valvotomy on Case 2; to my House Physicians, Drs. J. Monk and B. Gentin, for invaluable assistance with the patients investigated; Miss A. Dick for checking drafts and Messrs. Shevitz, Wetton and Schreve for photography and diagrams.

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NOTES AND NEWS · BERIGTE

THE NUTRITION SOCIETY OF GREAT BRITAIN

The symposium on *Man's Need for Water* arranged for Saturday, 23 March 1957, will be held at the rooms of the Royal Society of Medicine, 1 Wimpole Street, London, W.1.

On Saturdey, 20 April, the Annual Business Meeting of the Scottish Group and a symposium on *Clean Food* will be held in the University of Aberdeen.

On Friday, 3 May, the Annual General Meeting of the Nutrition Society will be held in London. In connexion with this there will also be a meeting for the presentation of original papers and demonstrations by members and others introduced by them.

* * *

Dr. L. J. A. Loewenthal, of Johannesburg, has recently been elected a Member of the British Association of Dermatology and an Honorary Member of the Dermatological Association of Australia.

* * *

EXPLOSION OF NUCLEAR BOMBS

Critic in the *New Statesman and Nation* of 9 February 1957, p. 162, discussing the reaction of Asians to the suggestion that H-bombs are being exploded at a high level to minimize the danger of the local 'fall-out' on the seas which provide the Japanese with their fish and on the vegetation which provides the Asians with their food, writes that the Japanese, who have made a special study of death-dust, are unlikely to be convinced by the assurances given. He adds:

'High level bursts aggregate the radioactive materials in the upper atmosphere so that they return to the earth's surface at the rate of 10 to 20 per cent a year. The strontium found in the bones of Britain's atom-age babies and in the bones of Welsh sheep browsing 12,000 miles from the testing grounds should remind us of that. By Operation Gadarene, as I've heard it called, the H-bomb powers are blindly following each other towards the precipice edge of radioactive "tolerance".'

* * *

ELI LILLY MEDICAL RESEARCH FELLOWSHIP (SOUTH AFRICA)

INCREASE IN THE VALUE OF THE AWARD

The Selection Committee of the Eli Lilly Medical Research Fellowship (South Africa) has been advised that the value of the South African Fellowship has been increased from $3,000 to $3,600 per year. This currency is payable to the Fellow in the United States in U.S. dollars during the tenure of his Fellowship.

In addition, the Fellow receives a travel allowance for the return first-class air fare from his place of residence in South Africa to his place of study in the U.S.A.

* * *

Dr. Jacob Adno, M.B., B.Ch., Dip. O. & G. (Rand), has commenced practice as an obstetrician and gynaecologist at 704 Medical Centre, Jeppe Street, Johannesburg. (Telephones: *Rooms*: 23-8491; *Residence*: 45-5436).

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